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Liver infarct masquerading as intrahepatic cholangiocarcinoma

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ABSTRACT

Cholangiocarcinoma is one of the most lethal tumors because of its complex location and lack of good chemoradiotherapy options. When it is diagnosed, urgent intervention is needed, often involving radical surgical resection. It generally presents as a liver mass with biliary obstruction. We discuss the case of a young patient presenting with liver dysfunction and imaging mimicking a liver mass concerning for cholangiocarcinoma, where he actually had a liver infarct from splanchnic venous thrombosis from primary myelofibrosis.

KEYWORDS Cholangiocarcinoma; liver mass; primary myelofibrosis

Cholangiocarcinomas arise from epithelial cells of bile ducts and typically present with a right upper quadrant mass and hepatic dysfunction. Myeloproliferative neoplasms are a group of clonal hematological malignancies characterized by thrombotic events and bone marrow failure syndromes and can present with thrombosis in unusual sites. We present a young patient presenting with a liver mass suggestive of cholangiocarcinoma that turned out to be an infarct from splanchnic venous thrombosis.

CASE REPORT

A previously healthy 32-year-old man presented to the hospital with right-sided abdominal pain, nausea, and vomiting for 24 hours. Physical examination disclosed right upper quadrant abdominal tenderness and tachycardia. Murphy's sign was negative. Initial labs showed transaminitis and indirect bilirubinemia *(Table 1)*. Lactate dehydrogenase was elevated, but hemoglobin and haptoglobin were within normal limits, with mild thrombocytosis. Computed tomography (CT) of the abdomen with contrast showed portal, splenic, and superior mesenteric vein thrombosis and a $7 \times 9 \times 10$ cm mass in the caudate lobe of the liver extending into the portal vein. The patient did not have any history of cirrhosis, hepatitis C, primary sclerosing cholangitis, or any other known liver disease. CT of the chest, abdomen/pelvis, and head did not show any evidence of other metastatic lesions. Magnetic resonance imaging (MRI) with liver mass protocol confirmed a heterogeneous mass showing gradual enhancement with gadolinium contrast—a pattern generally seen in cholangiocarcinoma or sometimes hepatocellular carcinoma *(Figure 1)*. Serum alpha-fetoprotein, carcinoembryonic antigen, and cancer antigen 19-9 levels were within normal range.

Suspecting cholangiocarcinoma, the hepatobiliary multidisciplinary team evaluated him for possible resection of the tumor, but the apparent involvement around the vessels made the tumor inoperable. CT-guided biopsy showed necrosis and hemorrhagic liver tissue in the sample. A second biopsy done with endoscopy and ultrasound guidance revealed the same appearance of necrosis and no confirmation of malignant cells by morphology or immunohistochemistry. Suspecting an infarct due to the necrosis in the tissue and venous thrombosis, a hypercoagulable disease workup was ordered, which revealed a Janus kinase 2 (JAK2) V617F mutation. He was started on anticoagulation with heparin, and a bone marrow biopsy showed a hypercellular bone marrow with features suggestive of primary

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Table 1. Pertinent laboratory values at diagnosis and after treatment

Laboratory test	Reference range	At diagnosis	After treatment
White blood cell count ($10^3/\mu L$)	4–11	5.8	4.2
Red blood cell count ($10^6/\mu L$)	4.1–5.6	4.87	4.3
Hemoglobin (g/dL)	12–17	14.1	13.8
Hematocrit (%)	35–49	40	39
Platelets ($10^3/\mu L$)	150–450	479	295
Total protein (g/dL)	6.4–8.6	6.4	6.6
Albumin (g/dL)	3.8–5.7	3.9	4.1
Bilirubin, total (mg/dL)	<1.0	3.8	0.7
Bilirubin, direct (mg/dL)	<0.4	0.8	0.1
Alkaline phosphatase (U/L)	34–104	232	141
Aspartate aminotransferase (U/L)	13–39	1709	27
Alanine aminotransferase (U/L)	7–52	2046	39
Lipase (IU/L)	11–82	31	
Lactate dehydrogenase (U/L)	140–271	690	187
Haptoglobin (mg/dL)	44–215	193	

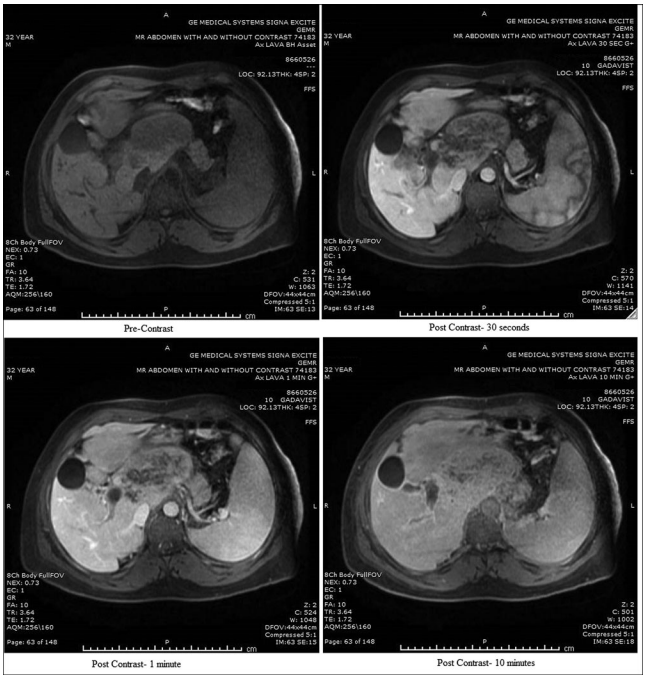

Figure 1. MRI of the abdomen with and without contrast at diagnosis showing a caudate lobe mass enhancing with contrast concerning for cholangiocarcinoma.

myelofibrosis (PMF) *(Figure 2)*. He was subsequently started on ruxolitinib and transitioned to oral anticoagulation.

Follow-up in 4 weeks showed remarkable improvement in liver function *(Table 1)*, and an MRI of the abdomen

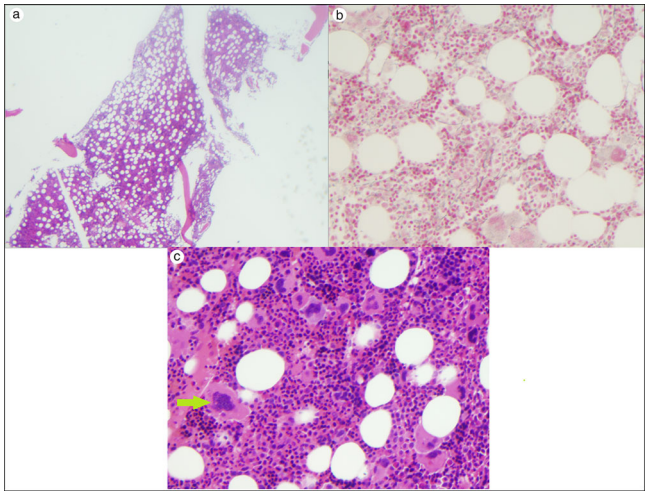

Figure 2. Bone marrow aspirate and biopsy showing features of primary myelofibrosis: **(a)** hypercellular bone marrow; **(b)** reticular fibrosis; and **(c)** hypercellular marrow with atypical megakaryocytes with hyperchromatic and hypo-segmented nuclei (arrow).

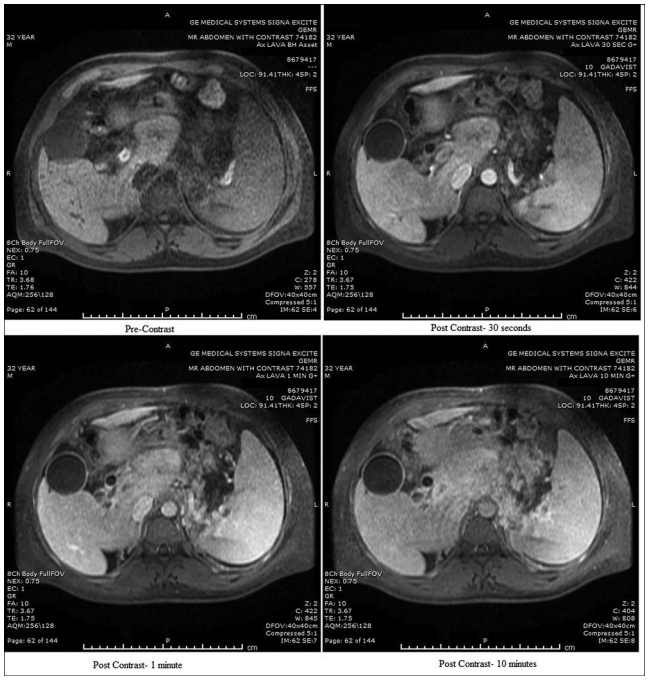

Figure 3. MRI of the abdomen with and without contrast after treatment showing improvement of the caudate lobe infarct.

showed a reduction in the size of the infarct as well as dissolution of the portal and splenic vein thrombosis *(Figure 3)*. The patient is currently being evaluated for a bone marrow transplant.

DISCUSSION

Cholangiocarcinomas are tumors with one of the worst survival rates due to the complexity of their location and poor response to conventional chemotherapies. They present with cholestasis and right upper quadrant mass and can be extra- or intrahepatic. Patients with malignancies

have a high risk of developing venous thromboembolic disease secondary to local tumor effects, procoagulant activity by tumor cells and host cells, immobility, surgery, and chemotherapy.[1,2] This risk is particularly high for gastrointestinal malignancies.[3]

The patient discussed in this case presented with typical signs of biliary obstruction, splanchnic vein thrombosis, and a liver mass strongly suggestive of intrahepatic cholangiocarcinoma. However, further evaluation revealed that the liver mass was actually an infarct secondary to thrombosis from PMF.

More than 70% of intrahepatic cholangiocarcinomas typically appear as hypodense hepatic lesions that enhance following contrast administration throughout arterial and venous phases.[4–6] Hepatocellular carcinoma, on the other hand, usually shows diffuse enhancement during the arterial phase of contrast administration and shows a washout during the delayed venous phase.[7] Liver infarcts typically appear as nonspecific lesions with hypointensity on T1 signal and hyperintensity on T2 signal.[8] Positron emission tomography can sometimes be helpful to distinguish between a malignant lesion and an infarct in doubtful liver masses, as an infarct will have low fluorodeoxyglucose uptake.

PMF is a stem cell–derived clonal neoplasm characterized by the proliferation of cellular components of myeloid lineage. The most commonly mutated genes found in PMF are *JAK2*, *CALR* (calreticulin), and *MPL* (myeloproliferative leukemia virus).[9] PMF is characterized by increased thrombotic tendency, hepatosplenomegaly, and extramedullary hematopoiesis.[10,11] The incidence of thrombotic events in PMF is 2 to 3 per 100 patient-years.[12] The thrombotic events in PMF are characteristic for occurring in "unusual" sites such as cerebral veins, splanchnic veins, and even in the arterial system.[13] Treatment of PMF is guided by the risk of disease progression and the presence of thromboses. The JAK2 inhibitors ruxolitinib or fedratinib along with hydroxyurea and anticoagulation form the mainstay of management. Allogeneic stem cell transplantation is the only treatment with the potential for cure in this disease.

In conclusion, this patient's presentation emphasizes that hepatic infarcts can give the appearance of a mass on imaging. Malignancies are known to increase the risk of thrombotic events, and a presentation as seen in this case can be easily misleading. This case highlights the vigilance needed to evaluate young patients with thrombosis in unusual sites like the splanchnic circulation in order to make the right diagnosis to prevent potentially harmful invasive or surgical intervention that could pose significant bleeding risks, as most patients with PMF will need systemic anticoagulation.

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